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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,134	10/10/2003	Hal S. Padgett	1328-005	1176

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EXAMINER
SHAW, AMANDA MARIE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

ttt

Office Action Summary	Application No.	Applicant(s)	
	10/684,134	PADGETT ET AL.	
	Examiner	**Art Unit**	
	Amanda M. Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-12,42 and 43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-12, and 42-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the amendment filed August 2, 2006. Applicant's arguments have been fully considered but are not persuasive to overcome all grounds of rejection. All rejections not reiterated herein are hereby withdrawn. This action is made final.

Claims 1, 4-5, and 7 have been amended. There are no new claims. Claims 1-2, 4-12, and 42-43 will be addressed herein.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4, and 6-8 remain rejected under 35 U.S.C. 102(b) as being anticipated by Chirikjian (WO 96/40902) for reasons of record set forth in the office aciton of April 26, 2006 and reiterated below.

Chirikjian et al teach a method for making a variant polynucleotide comprising: preparing at least one heteroduplex between at least said two parent polynucleotides, cleaving at least one polynucleotide strand in said heteroduplex at a mismatch site to form a cleavage site, replacing at least one nucleotide on at least one polynucleotide strand at or near the cleavage site, wherein at least one of said polynucleotide strands has a different nucleotide sequence from either of said at least two parent polynucleotides. Specifically Chirikjian et al teach a method wherein a single stranded probe is hybridized to a circular single stranded target polynucleotide. The probe is constructed so that it contains a single base that will form a mismatch with the target polynucleotide at a predetermined spot. The probe also contains fewer base sequences then the target polynucleotide so that hybridization results in a partially double stranded circular nucleic acid molecule (Page 26). The partially double stranded molecule is then converted into a complementary double stranded construct using DNA polymerase and ligase. The fully double stranded molecule is then treated with a nucleic acid repair enzyme which cleaves the target polynucleotide strand at the mismatch creating a gap in the target strand. Next the heteroduplex is transformed into a bacterium and in the process of the transformation; the gap created by the cleavage is filled with bases complementary to the exposed probe bases (Page 27).

Regarding Claim 2, Chirikjian et al teach that the polynucleotides forming the heteroduplex are circular. Specifically Chirikjian et al teach a method wherein a single stranded probe is hybridized to a circular single stranded target polynucleotide (Page 26).

Regarding Claim 4, Chirikjian et al teach a method wherein the heteroduplex polynucleotide sequence contains a gene. Specifically Chirikjian et al teach that single stranded DNA containing the gene sequence to be modified is allowed to hybridize with a synthetic oligonucleotide which is complementary to the region to be modified with a

Guanine mismatch at a position where the adenine is to be changed to a cytosine. Then the heteroduplex is treated with T4 DNA polymerase and T4 DNA ligase. The newly synthesized double stranded heteroduplex is then treated with mutY which cleaves the mismatch site. The material that is cleaved at the mismatch site is then transformed into E. coli and the gap created by the cleavage is closed (Page 33).

Regarding Claim 6, Chirikjian et al teach that the heteroduplex polynucleotide sequence is a region within a polynucleotide molecule of greater than about 100 bp. Specifically Chirikjian et al teach that the heteroduplex contained the p53 gene. The p53 gene is much larger than 100 bp (Page 33).

Regarding Claim 7, Chirikjian et al teach a method wherein at least three parental polynucleotides are used. Specifically Chirikjian et al teach that the method discussed above can also employ two probes that bind to the circular target. The first probe is complementary to a non mutated sequence in the target polynucleotide so that a mismatch will occur at the site of the point mutation in the target polynucleotide. The second probe is designed to hybridize to the target adjacent to the first probe (i.e. at a location such that the second probe is close enough to the first probe so that enzyme attached to the former can effect cleavage of the latter) (Page 15).

Regarding Claim 8, Chirikjian et al teach that a plurality of variant polynucleotides are formed. Specifically Chirikjian et al teach that the heteroduplex is transformed into a bacterium. It is inherent that the bacteria will produce multiple copies of the variant (Page 27).

RESPONSE TO ARGUMENTS

3. In the response filed August 2, 2006, Applicants traversed the rejection over Chirikjian by stating that the reference does not teach the generation of polynucleotide strands with different nucleotide sequences from the parent polynucleotides. Additionally the applicants argue that Chirikjian are not motivated to make variant sequences.

This argument has been fully considered but is not persuasive because the active process steps of the claimed method which include (i) preparing at least one heteroduplex between at least said two parent polynucleotides, (ii) cleaving at least one polynucleotide strand in said heteroduplex at a mismatch site to form a cleavage site, and (iii) replacing at least one nucleotide on at least one polynucleotide strand at or near the cleavage site are all taught by the Chirikjian reference. Additionally the method of Chirikjian produces a polynucleotide having a different sequence from either one of at least two parents. For example if one parent had the sequence of ATCGC and the second parent had the sequence of TAXCG where X could be C, A, or T and these two strands formed a heteroduplex and then the second parent strand was cleaved at position X and replaced with a nucleotide complementary to the first parent, the resulting sequence would be TAGCG. The specification defines the term "sequence variant" as a molecule (DNA, RNA polypeptide, and the like) with one or more sequence differences compared to a reference molecule. Hence the newly formed nucleotide (TAGCG) is different when compared to both parent sequences (which in this case are the reference sequences). Additionally the argument that Chirikjian is not motivated to make variant sequences is not a valid argument. Motivation is only argued over rejections under 35 U.S.C. 103.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 5 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Chirikjian (WO 96/40902) in view of Wetmur (US Patent 5877280) for reasons of record set forth in the office aciton of April 26, 2006 and reiterated below.

The teachings of Chirikjian et al are presented above in paragraph 2.

Regarding Claim 5, Chirikjian et al do not teach a method wherein the heteroduplex polynucleotide sequence is a genome.

However, Wetmur et al teaches a method called genome mismatch scanning. This method created for whole genome scanning utilizes E. coli MutS and the other enzymes of the mismatch repair system to detect differences between two strands of oligonucleotides (Column 12).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have applied the method of Chirikjian et al to an entire genome. One would have been motivated to do so in order to detect differences between two genomes which can then be applied towards genome mapping and or cloning genes based on sequence differences or similarities between the two genomes.

RESPONSE TO ARGUMENTS

5. In the response filed August 2, 2006, Applicants traversed the rejection over Chirikjian in view of Wetmur by stating that the Wetmur reference does not teach a method of preparing variant polynucleotides having a nucleotide sequence different from the parents.

This argument has been fully considered but is not persuasive because the Wetmur reference is not required to teach a method of preparing variant polynucleotides having a nucleotide sequence different from the parents because the Chirikjian reference does. In a proper 103 rejection a primary reference is provided which teaches most of the limitations and then a secondary reference is used to teach the limitations not taught by the primary reference. In the instant case the Chirikjian reference is the primary reference and it does in fact teach a method of preparing a variant polynucleotide that has a different nucleotide sequence from either of said at least two parent polynucleotides. The Wetmur reference has been applied here because the Chirikjian reference does not teach a method wherein the heteroduplex comprises an entire genome. However it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Chirikjian et al by using a heteroduplex that comprises the entire genome as suggested by Wetmur in order to detect point mutations in an entire genome.

6. Claims 9-12 and 42-43 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chirikjian (WO 96/40902) in view of Arnold (US 2002/0137661) for reasons of record set forth in the office aciton of April 26, 2006 and reiterated below.

The teachings of Chirikjian et al are presented above in paragraph 2.

Regarding Claim 9 and 43, Chirikjian et al do not teach screening or selecting a population of variants for a desired functional property.

However Arnold et al does teach screening or selecting a population of variants for a desired functional property. Specifically Arnold et al teaches a method for evolving a polynucleotide toward acquisition of a desired property. The methods involve at least two parent sequences that contain regions of similarity but also have regions of divergence. The two strands are hybridized to each other to form a heteroduplex. The heteroduplex is then exposed to enzymes of a DNA repair system and a replication system which can repair unmatched pairs. The resulting population is then screened for acquisition of a desired property. The property can be a property of the polynucleotide per se, such as capacity of a DNA molecule to bind to a protein or can be a property of an expression product thereof, such as mRNA or a protein (Page 4, Column 1).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Chirikjian et al so as to screened the population of variants in order to have achieved the benefits set forth by

Arnold of providing a method which allows for making variants which contain a desirable property and then screening for that property to make sure the variants actually have that property.

Regarding Claim 10, Chirikjian et al do not teach that a second heteroduplex comprising at least one variant strand can be formed and the process can be repeated.

However, Arnold et al teach that a second heteroduplex comprising at least one variant strand can be formed and the process can be repeated. Specifically Arnold et al teach that the variants can be subjected to further rounds of recombination using the heteroduplex procedures (Page 7, Column 1).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Chirikjian et al so as to repeated the process of making sequence variants using the variant generated in the first cycle in order to have achieved the benefits set forth by Arnold of providing a method which allows for multiple cycles of recombination. One would have been motivated to do this for the added benefit of making additional variants wherein each cycle creates a variant that is more variable than the original parent oligonucleotides.

Regarding Claims 11 and 12, Chirikjian et al do not teach that the variant polynucleotides can be converted to RNA and be translated prior to screening and selecting.

Arnold et al teach that the variant polynucleotides can be converted to RNA and be translated prior to screening and selecting. Specifically Arnold et al teach that the variant polynucleotides (DNA) as well as their expression products or secondary metabolites produced by their expression products are isolated a screened for the desired property (Page 7 Column 1). In order for the expression products to analyzed, the DNA would have had to been converted to RNA and then translated.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Chirikjian et al so as to have converted the variant polynucleotides to RNA and translated them prior to screening and selecting. For example, one benefit of doing this is that in cases where the desired functional property is a property of enzyme such as having a higher catalytic activity it would make sense to make sure that the RNA produced by the variant DNA molecule actually encoded and enzyme that had higher catalytic activity.

Regarding Claim 42, Chirikjian et al teach that the method can be carried out when the heteroduplex has at least two non complementary nucleotide base pairs. Specifically Chirikjian et al teach that the present invention comprehends the existence of multiple sites of mismatch on the heteroduplex (Page 11). However Chirikjian et al does not teach that the entire method is carried out in vitro. For example the step wherein the base pair gaps are filled in occurs in vivo.

However, Arnold et al teaches that the DNA repair step can be performed in vitro or in vivo. Arnold teaches that the heteroduplexes can be exposed to a DNA repair system in vitro. The DNA repair system can be obtained as extracts from repair competent E. Coli, yeast or any other cell. Repair competent cells are lysed in buffer and supplemented with nucleotides (Page 7, Column 1).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Chirikjian et al so that the step of DNA repair occurred in vitro. Arnold et al teach that in vitro DNA repair systems can be used as an alternative to in vivo repair systems.

RESPONSE TO ARGUMENTS

7. In the response filed August 2, 2006, Applicants traversed the rejection over Chirikjian in view of Arnold. Regarding Claims 9, 11-12 and 42-43 the applicants state that since Chirikjian does not generate a population of variants, there is no motivation to apply the screening technique of Arnold. Regarding Claim 10 applicants claim that Chirikjian is not motivated to repeat their process.

This argument has been fully considered but is not persuasive because the active process steps of the claimed method which include (i) preparing at least one heteroduplex between at least said two parent polynucleotides, (ii) cleaving at least one polynucleotide strand in said heteroduplex at a mismatch site to form a cleavage site, and (iii) replacing at least one nucleotide on at least one polynucleotide strand at or near the cleavage site are all taught by the Chirikjian reference. Additionally the method of Chirikjian produces a polynucleotide having a different sequence from either one of at least two parents. For example if one parent had the sequence of ATCGC and the second parent had the sequence of TAXCG where X could be C, A, or T and these two strands formed a heteroduplex and then the second parent strand was cleaved at position X and replaced with a nucleotide complementary to the first parent, the resulting sequence would be TAGCG. The specification defines the term "sequence variant" as a molecule (DNA, RNA polypeptide, and the like) with one or more sequence differences compared to a reference molecule. Hence the newly formed nucleotide (TAGCG) is different when compared to both parent sequences (which in this case are the reference sequences). Additionally the argument that Chirikjian is not motivated to repeat the process in not persuasive because the Arnold reference provides the motivation. Arnold et al teach a method which allows for multiple cycles of recombination in order to make additional variants wherein each cycle creates a variant that is more variable than the original parent oligonucleotides.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 1-2, 4-12, and 42-43 in the instant application are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-49, 51-64, and 69-71 of copending Application 10637758. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-2, 4-12, and 42-43 in the instant application are generic to all that is recited in claims 1-49, 51-64, and 69-71 of copending Application 10637758. That is, claims 1-2, 4-12, and 42-43 in the instant application fall entirely within the scope of claims 1-49, 51-64, and 69-71 of copending Application 10637758 or, in other words, claims 1-2, 4-12, and 42-43 in the instant application are anticipated by claims 1-49, 51-64, and 69-71 of copending Application 10637758. It is noted that the present claims are drawn to methods for preparing variant polynucleotides and methods for obtaining a polynucleotide sequence encoding a desired functional property. The claims of Application 10637758 are drawn to in vitro methods of making sequence variants, in vitro methods of increasing diversity in a population of sequences, methods of obtaining

a polynucleotide encoding a desired property, methods for altering the length of a polynucleic acid sequence, and methods of generating mutations in a zone around a particular nucleotide. As noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." Further, in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation." In the present situation, the method steps present are able to stand alone and the preamble limitation is not accorded patentable weight. Accordingly, the preamble merely sets forth the intended use of the method but does not limit the scope of the claims. Specifically, both sets of claims encompass methods comprising forming a heteroduplex between to polynucleotides, cleaving at least one polynucleotide at a mismatch site, and replacing at least one nucleotide at or near the cleavage site. The present claims differ from the claims of Application 10637758 in that the claims of Application 10637758 recite specific types of mismatch cleavage activity, proofreading activity, and ligase activity. However, the present claims are drawn to methods that recite the use of any reagent/enzyme that performs the functions of mismatch cleavage, proofreading and ligase activity. Thereby, the present claims are generic to the methods of 10637758 and encompass the limitations set forth in Application 10637758.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 1-2, 4-12, and 42-43 in the instant application are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application 10280913. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-2, 4-12, and 42-43 in the instant application are generic to all that is recited in claims 1-17 of copending Application 10280913. That is, claims 1-2, 4-12, and 42-43 in the instant application fall entirely within the scope of claims 1-17 of copending Application 10280913 or, in other words, claims 1-2, 4-12, and 42-43 in the instant application are anticipated by claims 1-17 of copending Application 10280913. It is noted that the present claims are drawn to methods for preparing variant polynucleotides and methods for obtaining a polynucleotide sequence encoding a desired functional property. The claims of Application 10280913 are drawn to in vitro methods of redistributing sequence

variations, an in vitro method of making a population of sequence variants. As noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." Further, in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation." In the present situation, the method steps present are able to stand alone and the preamble limitation is not accorded patentable weight. Accordingly, the preamble merely sets forth the intended use of the method but does not limit the scope of the claims. Specifically, both sets of claims encompass methods comprising forming a heteroduplex between to polynucleotides, cleaving at least one polynucleotide at a mismatch site, and replacing at least one nucleotide at or near the cleavage site. The present claims differ from the claims of Application 10280913 in that the claims of Application 10280913 recite that the two strands which form the heteroduplex are either 47%, 54% or 75% identical. However, the present claims are drawn to methods that recite that the heteroduplex has mismatched sites. Thereby, the present claims are generic to the methods of 10280913 and encompass the limitations set forth in Application 10280913.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 1-2, 4-12, and 42-43 in the instant application are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 66-72, 78-83, 85, 87-90 of copending Application 10066390. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-2, 4-12, and 42-43 in the instant application are generic to all that is recited in claims 66-72, 78-83, 85, 87-90 of copending Application 10066390. That is, claims 1-2, 4-12, and 42-43 in the instant application fall entirely within the scope of claims 66-72, 78-83, 85, 87-90 of copending Application 10066390 or, in other words, claims 1-2, 4-12, and 42-43 in the instant application are anticipated by claims 66-72, 78-83, 85, 87-90 of copending Application 10066390. It is noted that the present claims are drawn to methods for preparing variant polynucleotides and methods for obtaining a polynucleotide sequence encoding a desired functional property. The claims of Application 10066390 are drawn to in vitro methods of making linear sequence variants.

As noted in the MPEP 211.02, " a preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone." Further, in *Pitney Bowes Inc. v. Hewlett-Packard Co.*, 182F.3d 1298, 1305, 51 USPQ2d 1161, 1166 (Fed Cir. 1999) the court held that if the body of the claim sets forth the complete invention, and the preamble is not necessary to give "life, meaning and vitality" to the claim, "then the preamble is of no significance to claim construction because it cannot be said to constitute or explain a claim limitation." In the present situation, the method steps present are able to stand alone and the preamble limitation is not accorded patentable weight. Accordingly, the preamble merely sets forth the intended use of the method but does not limit the scope of the claims. Specifically, both sets of claims encompass methods comprising forming a heteroduplex between to polynucleotides, cleaving at least one polynucleotide at a mismatch site, and replacing at least one nucleotide at or near the cleavage site. The present claims differ from the claims of Application 10066390 in that the claims of Application 10066390 are specific for making linear sequence variants using in vitro methods. The present claims are drawn to methods of making circular and linear sequence variants using both in vitro and in vivo methods. Thereby, the present claims are generic to the methods of 10066390 and encompass the limitations set forth in Application 10066390.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

11. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER

Amanda M. Shaw
Examiner
Art Unit 1634